UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/005,684 | 11/08/2001 | Aristo Vojdani | IMSCI2.005A | 9590 |

20995 7590 12/19/2005

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

| EXAMINER | |
|---|---|
| YANG, NELSON C | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | |

DATE MAILED: 12/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/005,684 | VOJDANI, ARISTO | |
| | Examiner | Art Unit | |
| | Nelson Yang | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendment*

1. Applicant's amendment of claims 1, 2, and 12 is acknowledged and has been entered.

2. Claims 1-12 are currently pending.

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. With respect to claim 1, applicant recites the limitation that higher than normal levels of the second set but not the first set of a plurality of antibodies indicates the presence or possibility of autoimmune disease as well as the limitation that higher than normal levels of the second set but not the first set of a plurality of antibodies indicates ongoing pathology or early pathogenic reaction. It is unclear if these conditions are in the alternative or are inclusive of each other, rendering the claim indefinite.

6. With respect to claim 2, it is unclear if applicant intends to limit the second set of antibodies to a single antibody. Further clarification would be appreciated.

### *Claim Rejections - 35 USC § 112*

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

9. Applicant has recited that higher than normal levels of any of both the first set and second set of said plurality of antibodies or the first set but not the second set of said plurality of antibodies indicate the presence or possibility of autoimmune disease and cardiovascular disease. Furthermore, in claim 2, applicant appears to be further limiting the plurality of antibodies in the second set to a single antibody. However, according to Fig. 6, the presence or possibility of autoimmune disease and cardiovascular disease is only diagnosed when there are higher than normal levels of all the antibodies in both the first set and second set of said plurality of antibodies.

10. Furthermore, Applicant would only be able to determine the possibility or presence of the specific cardiovascular diseases for which the antigens are associated with. For example, higher than normal levels of myosin antibody would not necessarily suggest the presence or possibility of artherosclerosis, and normal levels of myosin antibody would not mean that there is no presence or possibility of cardiovascular disease and autoimmune disease. In fact there is no diagnosis made for higher than normal levels of any antibody in the first set but not the second set of antibodies. Indeed, the data present would appear to argue against the presence of

autoimmunity in this scenario. Yet claim 1 recites that this would indicate the presence or possibility of autoimmune disease and cardiovascular disease.

11. Although applicant provides data showing possible autoimmunity as well as data showing possible cardiovascular and autoimmune disease, applicant does not clearly disclose the steps of comparing the data to establish possible cardiovascular and autoimmune disease from possible autoimmune disease, or comparing the data to establish possible cardiovascular and autoimmune disease from possible autoimmunity.

12. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for a method for detecting antibodies against certain antigens and for indicating the presence or possibility of autoimmune disease, does not reasonably provide enablement for a method for distinguishing possible autoimmune disease from possible cardiovascular disease with autoimmune disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected to make or use the invention commensurate in scope with these claims. The specification, according page 24, merely refers to fig. 6 for diagnosing possible autoimmunity, and data interpretation of antibody levels to human target antigens relating to the possible autoimmunity. However, applicant has not provided any guidance on how to interpret the data presented in Fig. 6.

13. According to the data from figure 6, it is assumed that the levels of all 8 antigens would have to be measured in order to be able to distinguish between the likelihood of any autoimmune disease and the likelihood of any cardiovascular disease with any autoimmune disease. Applicants have only stated that "detection of above normal levels of saliva IgA antibody against the antigens listed in Figure 6 can help to diagnose possible autoimmunity" (pg. 0104). However,

in the claims, applicants have recited that "higher than normal levels of any of both the first set and second set of said plurality of antibodies" indicating that not all the antibodies need be at levels higher than normal. Futhermore, in claim 2, applicant appears to be further limiting the plurality of antibodies to a single antibody.

Although applicants have included the limitation of normal levels of the first and second set of said plurality of antibodies for indicating optimal conditions, there still appears to be some conflict remaining as toward diagnosing the medical condition of patients based on the information given in Fig. 6 and recited in the claims. For example, if there are normal levels of antibodies in the second set of antibodies, this would actually suggest the patient is in optimal condition, but only if the first set has normal levels of antibodies. However, if the first set has higher than normal levels of antibodies, the results would actually conflict with each other, as one set would indicate possible cardiovascular and autoimmune disease, whereas the other set would indicate optimal conditions, or at the very least, lack of autoimmunity. Specifically, the data presented in Figure 6, which suggests that lack of higher than normal levels of immune complexes, lupus peptide antibodies, and arthritic peptide antibodies would suggest a lack of possible autoimmunity, which appears to contradict claim 1, which recites that higher than normal levels of antibodies in the first set but not the second set would indicate the presence or possibility of cardiovascular disease **AND autoimmune disease**.

14. According to Strongin (Strongin, Sensitivity, specificity, and predictive value of diagnostic tests: definitions and clinical applications, 1993, Laboratory Diagnosis of Viral Infections, p. 211-219), a number of characteristics need to be considered in the development of any suitable diagnostic assay. These characteristics include the sensitivity of the assay, the true-

positive test rate, the false-negative test rate, the specificity, the true-negative test rate, the false positive test rate, the predictive value, the prevalence, the efficiency or percentage of all results that are true, and the accuracy of the recited diagnostic assay. However, none of these characteristics appear to have been considered.

Additional considerations must also be examined to enable the clinician to practice the invention, including assessment of when the maximum sensitivity, maximum specificity, and maximum efficiency are desired, how is the maximum sensitivity or specificity achieved, and how is the predictive value maximized. An essential understanding of these factors is required to enable the skilled artisan to accurately use and interpret any given diagnostic test. Specifically, the specification fails to disclose what is meant by the possibility of autoimmune disease or by the possibility of cardiovascular disease with autoimmune disease. Specifically, it is unclear how statistically significant are the results of this method.

### *Response to Arguments*

Applicant's amendment filed September 26, 2005 have been fully considered but they are not persuasive, as they do not appear to overcome all the rejections, as discussed above.

### *Conclusion*

15. No claims are allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

18. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
12/09/05